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Acute effects of ganglionated plexi ablation on sinoatrial nodal and atrioventricular nodal functions

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ABSTRACT

Ganglionated plexus (GP) ablation has been shown effective for eliminating atrial fibrillation (AF), the most common clinical tachyarrhythmia. However, the safety of destroying the main cardiac autonomic structures remains unclear. This study investigated the acute effects of GP ablation on the sinoatrial nodal (SAN) and atrioventricular nodal (AVN) functions in a canine model. In 10 open-chest dogs, multiple electrode catheters were sutured at both atria for recording and pacing. SAN and AVN function were evaluated. GP ablation caused no significant change of sinus rate immediately after GP ablation compared with the baseline state. After GP ablation, the sinus node recovery time (SNRT) and corrected SNRT did not show significant changes at long pacing cycle lengths (CLs), and only showed significant decrease at shorter pacing CLs. The AH interval at different pacing CLs, the Wenckebach atrioventricular block (AVB) CL, 2:1 AVB CL or the ventricular rate during AF were not significantly altered by GP ablations. Vagal suppression of SAN and AVN functions was eliminated by GP ablation. GP staining showed abundant choline acetyl transferase or tyrosine hydroxylase positive neurons. These findings suggest the functions of the SAN and AVN are mainly retained after GP ablation. These results may be partially related to destroying both parasympathetic and sympathetic elements in the GP by ablation.

1. Introduction

In 1998, Haïssaguerre et al. (1998) reported that most paroxysmal atrial fibrillation (AF) is initiated by ectopic beats originating from pulmonary veins (PVs); thereafter, catheter ablation targeting the PVs, i.e. PV isolation, has become the most popular strategy for eliminating AF. However, the risks of PV stenosis and esophageal injury, the relatively high recurrence rate and the requirement of more than 100 radiofrequency applications are the major limitations of PV isolation (Dagres et al., 2009). Recently, a serial of experimental studies (Lu et al., 2008b, 2009) suggest that activation of the intrinsic cardiac autonomic nervous system (ICANS) may contribute to the initiation of rapid firing from the PVs, and ablation of the main atrial fat pads containing ganglionated plexi (GP) may be effective in eliminating those PV firings (Po et al., 2006; Lu et al., 2008a). Clinical studies (Scherlag et al., 2005; Pokushalov et al., 2008; Po et al., 2009) also showed that GP ablation alone could reduce recurrence of AF not only in patients with "vagotonic AF" but also in those with "idiopathic or lone AF". Despite the benefits of GP ablation, the safety issue of GP ablation has not been evaluated although this ablation strategy has been applied in AF patients by several institutes (Pokushalov et al., 2008; Po et al., 2009). The autonomic nervous system plays an active role in the regulation of the sinoatrial nodal (SAN) and atrioventricular nodal (AVN) functions (Hou et al., 2007a, 2007b). Destruction of the main atrial autonomic elements by GP ablation may affect the functions of SAN and AVN and this raises several concerns for complications, such as sinus tachycardia and rapid ventricular rate during a recurrent AF. However, there is a lack of studies revealing the effects of GP ablation on the SAN and AVN functions.

Armour et al. (1997) and Pauza et al. (2000) performed elegant histological studies showing the location of autonomic ganglia on the atria in different species (Ardell and Randall, 1986; Vaitkevicius et al., 2009). The locations of major ganglia are substantially identical in the heart of human and large animal such as canine despite variable in shape, size and number of neurons (Pauza et al., 2002). In the present study, we aimed to investigate the acute effects of GP ablation on the SAN and AVN functions in a normal canine heart.

2. Methods

2.1. Animal preparation

All animal studies were reviewed and approved by the animal experimental administration of Wuhan University, China. The investigation conforms to the Guide for the Care and Use of Laboratory Animals published by the US National Institutes of Health (NIH

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Publication No. 85-23, revised 1996). Ten adult mongrel dogs weighing 18–25 kg were anesthetized with Na-pentobarbital, 30 mg/kg, and followed by additional dose of 2 mg/kg at the end of each hour. All dogs were ventilated with room air by a positive pressure respirator. Core body temperature was maintained at 36.5 ± 1.5 °C. The chest was entered via a left or right thoracotomy at the 4th intercostal space. Multi-electrode catheters were sutured to multiple sites to allow recording and pacing at the right atrium (RA), right superior pulmonary vein (RSPV) and right inferior pulmonary vein (RIPV) (Fig. 1A). Similar electrode catheters were sutured to the left atrium (LA), left superior pulmonary vein (LSPV) and left inferior pulmonary vein (LIPV, Fig. 1B). Another multipolar electrode catheter was positioned in the aortic root through the left femoral artery to record the His bundle electrogram (HBE). Both cervical vagal nerves were dissected and a pair of Teflon-coated silver wires (0.1 mm diameter) was inserted into each of the nerves for electrical stimulation by applying high frequency electrical stimulation (20 Hz, 0.1 ms duration, square waves, 0.6 to 8.0 V) (Hou et al., 2007b). To prevent drying and provide insulation from the surrounding tissues, the vagal nerves were immersed in a mixture of Vaseline and liquid paraffin. Standard ECG and blood pressure were continuously recorded. All tracings from the electrode catheters were amplified and digitally recorded using a computer-based Lab System (Lead 2000, Jingjiang Inc, China), filtered at 30 to 400 Hz. All pacing and stimulation were performed with a battery powered Medtronic stimulator (Model 5837).

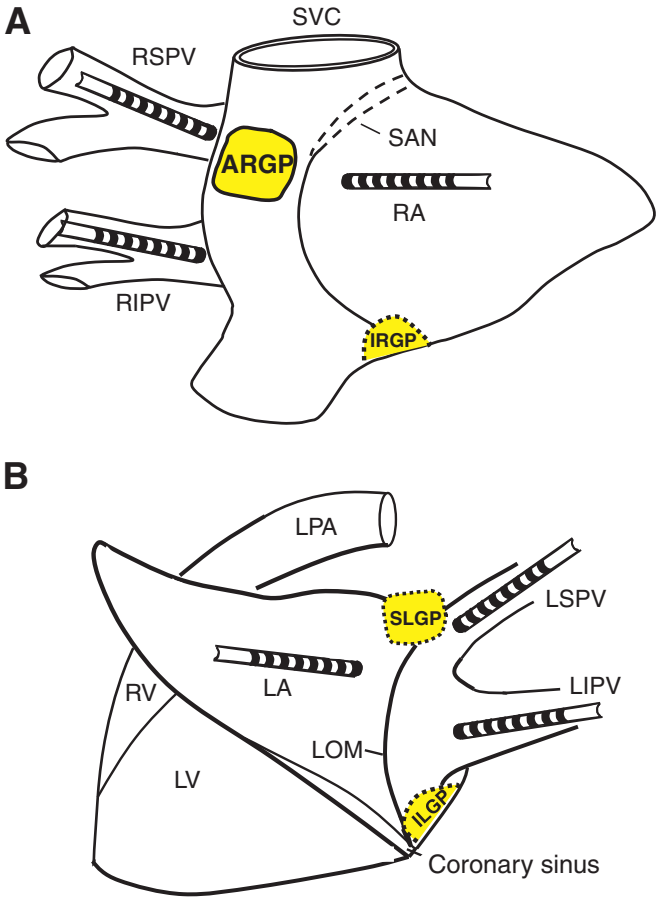

Fig. 1. Schematic representation and catheter position. (A) Right thoracotomy approach; (B) left thoracotomy approach. Multi-electrode catheters were sutured to the right superior PV (RSPV), right inferior PV (RIPV), right atrium (RA), left superior pulmonary vein (LSPV), left inferior PV (LIPV) and left atrium (LA). ARGP: anterior right ganglionated plexi; IRGP: inferior right GP; SLGP: superior left GP; ILGP: inferior left GP; LOM: ligament of Marshall; LV: left ventricle; RV: right ventricle; SVC: superior vena cava.

2.2. Evaluations of SAN and AVN functions

2.2.1. SAN function

The SAN function was evaluated by measurements of sinus node recovery time (SNRT) and corrected sinus node recovery time (cSNRT) during rapid pacing from the distal pair of RA catheter at 6 levels of decremental pacing cycle length (ms): 380, 350, 330, 300, 280 and 250. The pulse width of pacing was 2 ms and the strength was 2 times the pacing threshold. The duration of each episode of pacing lasted for 2 min and then was temporarily stopped for another 2 min before the next pacing period. In all experiments, determination of the SNRT was made by measuring the time from the last paced atrial complex to the following electrogram of spontaneous sinus beat. The cSNRT was determined by subtracting the average sinus cycle length following the RA pacing from the SNRT (Fig. 2A).

2.2.2. AVN function

The AVN function was evaluated by measurements of (1) Atrial-His (AH) interval at an incremental RA pacing; (2) the pacing cycle length (CL) at which Wenckebach AV block occurred (Fig. 3A) during incremental pacing (10 ms steps); (3) the pacing CL at which 2:1 AV block occurred (Fig. 3B) and (4) the average ventricular rate (VR) after AF was induced by burst pacing at the RA. AF was defined as irregular atrial rates faster than 500 bpm associated with irregular AV conduction lasting >5 s. The average VR during AF was determined by averaging the cycle lengths over the 10 ventricular beats of AF after it was induced by burst pacing.

2.3. GP ablation

Typically, there are 4 major left atrial GP located around the atrium in the human. Cardiac electrophysiologists have renamed these GP from the original description by Armour et al. and Pauza et al. based on their association with the PVs for easier communication during an ablation procedure. The superior left GP (SLGP) is located on the roof of the LA, near the LA–LSPV junction. The anterior right GP (ARGP) is located just anterior and inferior RSPV, in proximity to the junction of RSPV and both atria. The inferior left GP (ILGP) and inferior right GP (IRGP) are situated at the inferior aspect of the posterior wall of the left atrium. ILGP is located at the junction of LIPV and LA while the IRGP near the junction of inferior vein cava and both atria (Fig. 1).

The function of each GP was determined by applying high frequency electrical stimulation (HFS, 20 Hz, 0.1 ms duration, 0.6–4.5 V) with a big-tip (4 mm) electrode catheter. In this voltage range, progressive slowing of the heart rate (HR) or AV conduction was observed directly related to the voltage applied. Radiofrequency current (≤35 W) was immediately delivered at each site showing slowing of HR or AV conduction during HFS. In all cases, radio-frequency current was delivered to the epicardial surface of each GP. Complete ablation of each GP was verified by applying maximal strength of stimulation to the ablated area which failed to slow the sinus rate or inhibit AV conduction (Lu et al., 2008b, 2009)

2.4. Protocols

In 7 dogs, after obtaining the baseline recordings such as HR and AH intervals, the SAN and AVN functions were measured with and without bilateral cervical vagal stimulation prior to ablation. Bilateral vagal stimulation was set at the voltage required for slowing the sinus rate by 30%. After ablation of SLGP + ILGP and SLGP + ILGP + ARGP + IRGP, the above measurements of SAN and AVN functions with and without vagal stimulation were repeated, and the results were compared to those obtained prior to GP ablation. The voltage for vagal stimulation after GP ablation was set at the same voltage as prior to ablation. All the subsequent measurements after GP ablation or